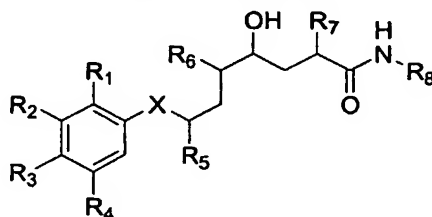


CLAIMS

We claim:

1. A method for the treatment or prevention of
 5 Alzheimer's disease, mild cognitive impairment Down's syndrome,
 Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-
 Type, cerebral amyloid angiopathy, other degenerative dementias,
 dementias of mixed vascular and degenerative origin, dementia
 associated with Parkinson's disease, dementia associated with
 10 progressive supranuclear palsy, dementia associated with
 cortical basal degeneration, diffuse Lewy body type of
 Alzheimer's disease comprising administration of a
 therapeutically effective amount of a compound or salt of
 formula 1 to a subject in need thereof:



formula 1

wherein

- R₁ is hydrogen, hydroxy, lower alkoxy, cycloalkoxy, lower
 alkoxy-lower alkoxy or free or esterified or amidated
 20 carboxy-lower alkoxy;
 R₂ is hydrogen, lower alkyl, cycloalkyl, lower alkoxy-lower
 alkyl, lower alkoxy-lower alkoxy-lower alkyl, cycloalkoxy-
 lower alkyl, hydroxy, optionally lower alkanoylated,
 halogenated or sulfonylated hydroxy-lower alkoxy; amino-
 25 lower alkyl that is unsubstituted or substituted by lower
 alkyl, by lower alkanoyl and/or by lower alkoxycarbonyl;
 optionally hydrogenated heteroaryl-lower alkyl; amino-lower
 alkoxy that is substituted by lower alkyl, by lower
 alkanoyl and/or by lower alkoxycarbonyl; oxo-lower alkoxy,

lower alkoxy, cycloalkoxy, lower alkenyloxy, cycloalkoxy-
lower alkoxy, lower alkoxy-lower alkoxy, lower alkoxy-lower
alkenyl, lower alkenyloxy-lower alkoxy, lower alkoxy-lower
alkenyloxy, lower alkenyloxy-lower alkyl, lower alkanoyl-
5 lower alkoxy, optionally S-oxidised lower alkylthio-lower
alkoxy, lower alkylthio-(hydroxy)-lower alkoxy, aryl-lower
alkoxy, optionally hydrogenated heteroaryl-lower alkoxy,
cyano-lower alkoxy, free or esterified or amidated carboxy-
lower alkoxy or free or esterified or amidated carboxy-
10 lower alkyl;

R₃ is halogenated lower alkyl, lower alkoxy-lower alkyl,
cycloalkoxy-lower alkyl, hydroxy-lower alkyl, optionally S-
oxidised lower alkylthio-lower alkyl, optionally
hydrogenated heteroarylthio-lower alkyl, optionally
15 hydrogenated heteroaryl-lower alkyl; amino-lower alkyl that
is unsubstituted or N-mono- or N,N-di-lower alkylated. N-
lower alkanoylated or N-lower alkane-sulfonylated or N,N-
disubstituted by lower alkylene, by unsubstituted or N'-
lower alkylated or N'-lower alkanoylated aza-lower
20 alkylene, by oxa-lower alkylene or by optionally S-oxidised
thia-lower alkylene; cyano-lower alkyl, free or esterified
or amidated carboxy-lower alkyl, cycloalkyl, aryl, hydroxy,
lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy,
cycloalkoxy-lower alkoxy, hydroxy-lower alkoxy, aryl-lower
25 alkoxy, optionally halogenated lower alkoxy, optionally S-
oxidised lower alkylthio-lower alkoxy, optionally
hydrogenated heteroaryl-lower alkoxy, optionally
hydrogenated heteroarylthio-lower alkoxy; amino-lower
alkoxy that is unsubstituted or N-mono- or N,N-di-lower
30 alkylated. N-lower alkanoylated or N-lower
alkanesulfonylated or substituted by lower alkylene, by
unsubstituted or N'-lower alkylated or N'-lower
alkanoylated aza-lower alkylene, by oxa-lower alkylene or

by optionally S-oxidised thia-lower alkylene; cyano-lower alkoxy or free or esterified or amidated carboxy-lower alkoxy;

5 R_4 is hydrogen, lower alkyl, hydroxy, lower alkoxy or cycloalkoxy;

X is methylene;

R_5 is lower alkyl or cycloalkyl;

R_6 is unsubstituted or N-mono- or N,N-di-lower alkylated or N-lower alkanoylated amino;

10 R_7 is lower alkyl, lower alkenyl, cycloalkyl or aryl-lower alkyl; and

R_8 is lower alkyl, cycloalkyl, free or aliphatically esterified or etherified hydroxy-lower alkyl; amino-lower alkyl that is unsubstituted or N-lower alkanoylated or N-mono- or N,N-di-lower alkylated or N,N-disubstituted by lower alkylene, by hydroxy-, lower alkoxy- or lower alkanoyloxy-lower alkylene, by unsubstituted or N'-lower alkanoylated or N'-lower alkylated aza-lower alkylene, by oxa-lower alkylene or by optionally S-oxidised thia-lower alkylene; free or esterified or amidated carboxy-lower alkyl, free or esterified or amidated dicarboxy-lower alkyl, free or esterified or amidated carboxy-(hydroxy)-lower alkyl, free or esterified or amidated carboxycycloalkyl-lower alkyl, cyano-lower alkyl, lower alkanesulfonyl-lower alkyl, 20 unsubstituted or N-mono- or N,N-di-lower alkylated thiocarbamoyl-lower alkyl, unsubstituted or N-mono- or N,N-di-lower alkylated sulfamoyl-lower alkyl, or a heteroaryl radical bonded via a carbon atom and optionally hydrogenated and/or oxo-substituted, or lower alkyl 25 substituted by a heteroaryl radical bonded via a carbon atom and optionally hydrogenated and/or oxo-substituted, or 30 a pharmaceutically acceptable salt thereof. .

2. A method according to claim 1 wherein

R₁ is hydrogen, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy or N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy;

R₂ is hydrogen, lower alkyl, cycloalkyl, lower alkoxy-lower alkyl, lower alkoxy-lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, hydroxy, lower alkanoyloxy-lower alkyl, hydroxy-lower alkoxy, halo-(hydroxy)-lower alkoxy, lower alkane-sulfonyl-(hydroxy)-lower alkoxy, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, lower alkanoylamino-lower alkyl, lower alkoxycarbonylamino-lower alkyl, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, lower alkanoylamino-lower alkoxy, lower alkoxycarbonylamino-lower alkoxy, oxo-lower alkoxy, lower alkoxy, cycloalkoxy, lower alkenyloxy, cycloalkoxy-lower alkoxy, lower alkoxy-lower alkoxy, lower alkoxy-lower alkenyl, lower alkenyloxy-lower alkoxy, lower alkoxy-lower alkenyloxy, lower alkenyloxy-lower alkyl, lower alkanoyl-lower alkoxy, lower alkylthio-lower alkoxy, lower alkanesulfonyl-lower alkoxy, lower alkylthio-(hydroxy)-lower alkoxy, aryl-lower alkoxy, thiazolylthio-lower alkoxy or thiazolinylthio-lower alkoxy, imidazolylthio-lower alkoxy, optionally N-oxidised pyridylthio-lower alkoxy, pyrimidinylthio-lower alkoxy, cyano-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, N-mono- or N, N-all-lower alkylcarbamoyl-lower alkoxy, carboxy-lower alkyl, lower alkoxy-carbonyl-lower alkyl, carbamoyl-lower alkyl or N-mono- or N,N-di-lower alkyl-carbamoyl-lower alkyl;

R₃ is lower alkyl, polyhalo-lower alkyl, lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, hydroxy-lower alkyl, lower

alkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, optionally partially hydrogenated or N-oxidised pyridyl-lower alkyl, thiazolylthio-lower alkyl or thiazolinylthio-lower alkyl, imidazolylthio-lower alkyl, optionally N-oxidised pyridylthio-lower alkyl, pyrimidinylthio-lower alkyl, amine-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, lower alkanoylamino-lower alkyl, lower alkanesulfonylamino-lower alkyl, polyhalo-lower alkanesulfonylamino-lower alkyl, pyrrolidino-lower alkyl, piperidino-lower alkyl, piperazino-, N'-lower alkylpiperazino- or N'-lower alkanoylpiperazino-lower alkyl, morpholino-lower alkyl, thiomorpholino-. S-oxothiomorpholino- or S,S-dioxothiomorpholino-lower alkyl, cyano-lower alkyl, carboxy-lower alkyl, lower alkoxy-carbonyl-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkyl, cycloalkyl; phenyl or naphthyl that is unsubstituted or mono-, di- or tri-substituted by lower alkyl, lower alkoxy, hydroxy, lower alkylamino, di-lower alkylamino, halogen and/or by trifluoromethyl; hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, cycloalkoxy-lower alkoxy, hydroxy-lower alkoxy; phenyl-lower alkoxy or naphthyl-lower alkoxy that is unsubstituted or mono-, di- or tri-substituted by lower alkyl, lower alkoxy, hydroxy, lower alkylamino, di-lower alkylamino, halogen and/or by trifluoromethyl; lower alkoxy, polyhalo-lower alkoxy, lower alkylthio-lower alkoxy, lower alkanesulfonyl-lower alkoxy, optionally hydrogenated heteroaryl-lower alkoxy, optionally partially or fully hydrogenated hetero-arylthio-lower alkoxy, such as thiazolylthio-lower alkoxy or thiazolinylthio-lower alkoxy, imidazolylthio-lower alkoxy, optionally N-oxidised pyridylthio-lower alkoxy, pyrimidinylthio-lower alkoxy, amine-lower alkoxy, lower alkylamino-lower alkoxy, di-lower

alkylamino-lower alkoxy, lower alkanoylamino-lower alkoxy,
lower alkanesulfonylamino-lower alkoxy, polyhalo-lower
alkanesulfonylamino-lower alkoxy, pyrrolidino-lower alkoxy,
piperidino-lower alkoxy, piperazino-, N'-lower
5 alkylpiperazino- or N'-lower alkanoylpiperazino-lower
alkoxy, morpholino-lower alkoxy, thiomorpholino-, S-
oxothiomorpholino-or S,S-dioxothiomorpholino-lower alkoxy,
cyano-lower alkoxy, carboxy-lower alkoxy, lower
alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy or N-
10 mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy;
R₄ is hydrogen, lower alkyl, hydroxy, lower alkoxy or
cycloalkoxy;
X is methylene;
R₅ is lower alkyl or cycloalkyl;
15 R₆ is amino, lower alkylamino, di-lower alkylamino or lower
alkanoylamino;
R₇ is lower alkyl, lower alkenyl, cycloalkyl, or phenyl- or
naphthyl-lower alkyl that is unsubstituted or mono-, di- or
tri-substituted by lower alkyl, lower alkoxy, hydroxy,
20 lower alkylamino, di-lower alkylamino, halogen and/or by
trifluoromethyl; and
R₈ is lower alkyl, cycloalkyl, hydroxy-lower alkyl, lower
alkanoyloxy-lower alkyl, lower alkoxy-lower alkyl or lower
alkenyloxy-lower alkyl, amino-lower alkyl, lower
25 alkanoylamino-lower alkyl. N-mono- or N,N-di-lower
alkylamino-lower alkyl, optionally hydroxylated or lower
alkoxylated piperidino-lower alkyl, such as piperidino-
lower alkyl, hydroxypiperidino-lower alkyl or lower alkoxy-
piperidino-lower alkyl, piperazino-, N'-lower
30 alkylpiperazino- or N'-lower alkanoylpiperazino-lower
alkyl, unsubstituted or lower alkylated morpholino-lower
alkyl, such as morpholino-lower alkyl or
dimethylmorpholino-lower alkyl, or optionally S-oxidised

thiomorpholino-lower alkyl, such as thiomorpholino-lower alkyl, S,S-dioxothiomorpholino-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkyl, dicarboxy-lower alkyl, di-lower alkoxycarbonyl-lower alkyl, dicarbamoyl-lower alkyl, di-(N-mono- or N,N-di-lower alkylcarbamoyl)-lower alkyl, carboxy-(hydroxy)-lower alkyl, lower alkoxy-carbonyl-(hydroxy)-lower alkyl or carbamoyl-(hydroxy)-lower alkyl, cyano-lower alkyl, lower alkanesulfonyl-lower alkyl, sulfamoyl-lower alkyl, lower alkyl-sulfamoyl-lower alkyl, di-lower alkylsulfamoyl-lower alkyl, thiocarbamoyl-lower alkyl, lower alkylthiocarbamoyl-lower alkyl, di-lower alkylthiocarbamoyl-lower alkyl, pyrrolidinyl, imidazolyl, benzimidazolyl, oxadiazolyl, pyridyl, oxopiperidinyl, quinolinyl, unsubstituted or N-lower alkanoylated piperidyl or pyrrolidinyl, imidazolyl-lower alkyl, benzimidazolyl-lower alkyl, oxadiazolyl-lower alkyl, pyridyl-lower alkyl, unsubstituted or N-lower alkanoylated piperidyl-lower alkyl or pyrrolidinyl-lower alkyl, oxopiperidinyl-lower alkyl, quinolinyl-lower alkyl, morpholinocarbonyl-lower alkyl or unsubstituted or N-lower alkanoylated piperidyl-lower alkyl, or a pharmaceutically acceptable salt thereof. .

3. A method according to claim 1 wherein

R₁ is hydrogen;

R₂ is lower alkyl, lower alkoxy-lower alkyl, lower alkoxy-lower alkoxy, lower alkoxy-tower alkoxy-lower alkyl; phenyl-lower alkoxy that is unsubstituted or substituted by lower alkyl, lower alkoxy, hydroxy, halogen, nitro and/or by amino; optionally N-oxidised pyridyl-lower alkoxy, lower alkylthio-lower alkoxy, lower alkanesulfonyl-lower alkoxy, lower alkanoyl-lower alkoxy, optionally N-oxidised pyridyl-

lower alkoxy, cyano-lower alkoxy, carboxy-lower alkoxy,
lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy,
lower alkylcarbamoyl-lower alkoxy or di-lower
alkylcarbamoyl-lower alkoxy,

5 R₃ is hydrogen, lower alkyl, hydroxy, lower alkoxy or polyhalo-
lower alkoxy,

R₄ is hydrogen or together with R₃ is lower alkylidenedioxy,

X is methylene,

R₅ is lower alkyl or cycloalkyl;

10 R₆ is amine, lower alkylamino, di-lower alkylamino or lower
alkanoylamino,

R₇ is lower alkyl, and

R₈ is lower alkyl, hydroxy-lower alkyl, lower alkanoyl-lower
alkyl, lower alkoxy-lower alkyl, lower alkenyloxy-lower
15 alkyl, amino-lower alkyl, lower alkanoyl-amino-lower alkyl,
such as 2-(C₁-C₄ alkanoylamino)-2-methyl-propyl, such as 2-
acetylamino-2-methyl-propyl or 2-formylamino-2-methyl-
propyl, N-mono- or N,N-di-lower alkylamino-lower alkyl,
piperidino-lower alkyl, hydroxypiperidino-lower alkyl,
20 lower alkoxypiperidino-lower alkyl, morpholino-lower alkyl,
dimethylmorpholino-lower alkyl, thiomorpholino-lower alkyl.
S,S-dioxothiomorpholino-lower alkyl, Carboxy-lower alkyl,
lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, N-
mono- or N,N-di-lower alkylcarbamoyl-lower alkyl, carboxy-
25 (hydroxy)-lower alkyl, lower alkoxycarbonyl-(hydroxy)-lower
alkyl, carbamoyl-(hydroxy)-lower alkyl, 5- or 6-membered
carboxycycloalkyl-lower alkyl, 5- or 6-membered lower
alkoxycarbonylcycloalkyl-lower alkyl. 5- or 6-membered
carbamoylcycloalkyl-lower alkyl, 5- or 6-membered N-mono-
30 or N, N-di-lower alkylcarbamoylcycloalkyl-lower alkyl,
cyano-lower alkyl, lower alkanesulfonyl-lower alkyl,
sulfamoyl-lower alkyl, lower alkylsulfamoyl-lower alkyl or
di-lower alkylsulfamoyl-lower alkyl, imidazolyl-lower

alkyl, oxopyrrolidinyl-lower alkyl, benzimidazolyl-lower alkyl, oxadiazolyl-lower alkyl, pyridyl-lower alkyl, oxopiperidinyl-lower alkyl or quinolinyl-lower alkyl, piperidin-4-yl-lower alkyl or 1-C₁-C₇-lower alkanoylpiperidin-4-yl-lower alkyl, or a pharmaceutically acceptable salt thereof. .

4. A method according to claim 1 wherein

R₁ and R₄ are hydrogen;

10 R₂ is C₁-C₄ alkoxy- C₁-C₄ alkoxy or C₁-C₄ alkoxy- C₁-C₄ alkyl;

R₃ is C₁-C₄ alkyl or C₁-C₄ alkoxy;

R₆ is amino;

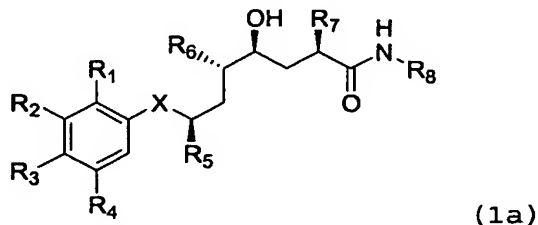
X is methylene;

R₅ and R₇ are branched C₁-C₄ alkyl; and

15 R₈ is carbamoyl- C₁-C₄ alkyl, N-C₁-C₄ alkylcarbamoyl- C₁-C₄ alkyl, N,N-di- C₁-C₄ alkyl-carbamoyl- C₁-C₄ alkyl, morpholino- C₁-C₄ alkyl, thiomorpholino- C₁-C₄ alkyl, 4-(1- C₁-C₄ alkanoylpiperidyl)- C₁-C₄ alkyl or 2-oxopyrrolidinyl- C₁-C₄ alkyl, or a pharmaceutically acceptable salt thereof. .

20

5. A method according to claim 1 wherein at least one asymmetric carbon atom of the main chain has the stereochemical configuration shown in formula 1a



25 each of the variables being as defined in claim 1, or a pharmaceutically acceptable salt thereof.

6. A method according to claim 1 wherein the compound is selected from the group consisting of:

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (p-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -ethyl-8- (p-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

5 2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -methyl-8- (4-biphenyl)-octanoic acid (N-butyl)amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amine-7 (S) -isopropyl-8- (3-hydroxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

10 2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (2-hydroxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (3-ethoxycarbonylmethoxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

15 2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (3-allyloxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (3-methoxycarbonyl-allyloxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

20 2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (3-methoxycarbonyl-methoxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (3-carbamoyl-methoxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

25 2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-(pyrid-2-yl-methoxy)-4-tert-butyl-phenyl]-octanoic acid (N-butyl)amide;

30 2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-(pyrid-4-yl-methoxy)-4-tert-butyl-phenyl]-octanoic acid (N-butyl)amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-(N-oxido-pyrid-2-yl-methoxy)-4-tert-butyl-phenyl]-octanoic acid (N-butyl)amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(2-ethoxycarbonylallyl-oxy) -4-tert-butyl-phenyl]-octanoic acid
(N-butyl) amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
5 (2-ethoxycarbonyl-propyloxy) -4-tert-butyl-phenyl]-octanoic acid
(N-butyl) amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(methylthio-methoxy) -4-tert-butyl-phenyl]-octanoic acid (N-
butyl) amide;

10 2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(methylsulfonyl-methoxy) -4-tert-butyl-phenyl]-octanoic acid (N-
butyl) amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(carboxy-methoxy) -4-tert-butyl-phenyl]-octanoic acid (N-
15 butyl) amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(3,3-dimethyl-2-oxo-butyloxy) -4-tert-butyl-phenyl]-octanoic acid
(N-butyl) amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
20 (2-nitrobenzyloxy) 4-tert-butyl-phenyl]-octanoic acid (N-
butyl) amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(2-aminobenzyloxy) -4-tert-butyl-phenyl]-octanoic acid (N-
butyl) amide;

25 2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(3-chloro-2 (R) hydroxypropyloxy) -4-tert-butyl-phenyl]-octanoic
acid (N-butyl) amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(3-methylthio-2 (S,R) -hydroxypropyloxy) -4-tert-butyl-phenyl]-
30 octanoic acid (N-butyl) amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(3-methylsulfonyl- (S,R) -hydroxypropyloxy) -4-tert-butyl-phenyl]-
octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(methylsulfonyl-methoxy) -4-tert-butyl-phenyl] -octanoic acid (N-
3-morpholino-propyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (3-
5 methoxycarbonyl-methoxy-phenyl) -octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(methoxycarbonyl-methoxy) -4-methoxy-phenyl] -octanoic acid (N-
butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (N-
10 methyl-carbamoyl-methoxy) -4-methoxy-phenyl] -octanoic acid (N-
butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (3-
methylsulfonyl-propyloxy) -4-methoxy-phenyl] -octanoic acid (N-
butyl) amide;

15 2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(methylsulfonyl-methoxy) -4-methoxy-phenyl] -octanoic acid (N-
butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (3-
methoxy-propyloxy) -4-methoxy-phenyl] -octanoic acid (N-
20 butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (2-
methoxy-ethoxy) -4-methoxy-phenyl] -octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (3-
hydroxy-propyloxy) -4-methoxy-phenyl] -octanoic acid (N-
25 butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(carbamoylmethoxy) -4-methoxy-phenyl] -octanoic acid (N-
butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (3-
30 cyanomethoxy-4-methoxy-phenyl) -octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (4-
methoxy-butoxy) -4-methoxy-phenyl] -octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (2-ethoxy-ethoxy) -4-methoxy-phenyl] -octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- {3- [2- (2-methoxy-ethoxy) -ethoxy] -4-methoxy-phenyl} -octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (3-pentyloxy-4-methoxy-phenyl) -octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (3-benzyloxy-4-methoxy-phenyl) -octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (3-ethoxy-propyloxy) -4-methoxy-phenyl] -octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (pyrid-4-ylmethoxy) -4-methoxy-phenyl] -octanoic acid (N-butyl) amide;

2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (2-ethoxycarbonyl-methoxy-4-tert-butyl-phenyl) -octanoic acid (N-butyl) amide;

2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (2-ethoxycarbonyl-4-tert-butyl-phenyl) -octanoic acid (N-butyl) amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4- (3-hydroxypropyloxy) -3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carbamoyl-2, 2-dimethyl-ethyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-isopropyl-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carbamoyl-2, 2-dimethyl-ethyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-tert-butyl-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carbamoyl-2, 2-dimethyl-ethyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4- (3-methylsulfonyl-propyloxy) -3- (3-methoxy-propyloxy) -phenyl] -octanoic acid (N-2-morpholinoethyl) amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4- (3-methylsulfonyl-propyloxy) -3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carbamoyl-2,2-dimethyl-ethyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [3,4-di (3-hydroxypropyloxy) -phenyl] -octanoic acid (N-2-morpholinoethyl) amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [3,4-di (3-hydroxypropyloxy) -phenyl] -octanoic acid [N- (2-carbamoyl-2,2-dimethyl-ethyl)] -amide;

10 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4- (3-N-methylcarbamoyl-propyl) -3- (3-methoxy-propyloxy) -phenyl] -octanoic acid (N-2-morpholinoethyl) amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4- (2-morpholinoethoxy) -3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carbamoyl-2,2-dimethyl-ethyl)] -amide;

15 [5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [3- (3-methoxypropyloxy) -4,5-ethylenedioxy-phenyl] -octanoic acid (N-2-morpholinoethyl) amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [3- (3-methoxypropyloxy) -4,5-ethylenedioxy-phenyl] -octanoic acid [N- (2-carbamoyl-2,2-dimethyl-ethyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [3- (3-methoxy-propyloxy) -4,5-methylenedioxy-phenyl] -octanoic acid (N-2-morpholinoethyl) amide;

25 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [3- (3-methoxypropyloxy) -4,5-methylenedioxy-phenyl] -octanoic acid [N- (2-carbamoyl-2,2-dimethyl-ethyl)] amide;]

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carbamoyl-2,2-ethylene-ethyl)] -amide;

30 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propoxy) -phenyl] -octanoic acid [N- (3 (S) -2-oxo-pyrrolidin-3-yl-methyl)] amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (4-methoxy-but-2-eneoxy) -phenyl] -octanoic acid (N-butyl) amide;

5 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-hydroxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid (N-butyl) amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8-H-benzyloxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid (N-butyl) amide;

10 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [3,4-di (3-methoxypropyloxy) -phenyl] -octanoic acid (N-butyl) amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4- (2,2,2-trifluoroethoxy) -3- (3-methoxypropyloxy) -phenyl] -octanoic acid (N-butyl) amide;

15 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4- (3-hydroxy-propyloxy) -3- (3-methoxypropyloxy) -phenyl] -octanoic acid (N-butyl) amide;

20 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4- (2-amino-ethoxy) -3- (3-methoxypropyloxy) -phenyl] -octanoic acid (N-butyl) amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4- (5-amino-pentyloxy) -3- (3-methoxypropyloxy) -phenyl] -octanoic acid (N-butyl) amide;

25 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4- (4-amino-butyloxy) -3- (3-methoxypropyloxy) -phenyl] -octanoic acid (N-butyl) amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4- (4-N,N-dimethylamino-butyloxy) -3- (3-methoxypropyloxy) -phenyl] -octanoic acid (N-butyl) amide;

30 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- {4- [4-N- (trifluoromethane-sulfonylaminobutyloxy) -3- (3-methoxypropyloxy) -phenyl] } -octanoic acid (N-butyl) -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 - [4 -
carboxymethoxy-3 - (3-methoxypropyloxy) -phenyl] -octanoic acid (N-
butyl) amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 - [4 - (3 -
5 ethoxycarbonyl-propyloxy) -3 - (3-methoxy-propyloxy) -phenyl] -
octanoic acid (N-butyl) amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 - [4 - (3 -
carboxy-propyloxy) -3 - (3-methoxypropyloxy) -phenyl] -octanoic acid
(N-butyl) amide;

10 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 - [4 - (4 -
methoxycarbonylbutyloxy) -3 - (3-methoxypropyloxy) -phenyl] -octanoic
acid (N-butyl) amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 - [4 - (4 -
carboxy-butyloxy) -3 - (3-methoxypropyloxy) -phenyl] -octanoic acid
15 (N-butyl) amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8 - [4-methoxy-
3 - (3-methoxy-propyloxy) -phenyl] -octanoic acid (N-butyl) amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8 - [4-methoxy-
3 - (2-methoxymethoxy-ethyl) -phenyl] -octanoic acid (N-butyl) amide;

20 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8 - [4 - (3 -
hydroxypropyloxy) -3 - (methoxypropyloxy) -phenyl] -octanoic acid N-
(2-morpholinoethyl) amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 - [4 -
methoxy-3 - (3-methoxy-propyloxy) -phenyl] -octanoic acid N - [2 - (4 -
25 hydroxypiperidin-1-yl) ethyl] amide dihydrochloride;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 - [4 -
methoxy-3 - (3-methoxy-propyloxy) -phenyl] -octanoic acid N - [2 -
(trans-2,6-dimethyl-morpholino) ethyl] amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 - [4 -
30 methoxy-3 - (3-methoxypropyloxy) -phenyl] -octanoic acid N - [2 - (cis-
2,6-dimethyl-morpholino) ethyl] amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- (2-piperidinoethyl) amide;

5 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- [2- (4-methoxypiperidino) -ethyl] -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- (2-thiomorpholinoethyl) amide;

10 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (3-hydroxypropyl)] amide;

15 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (4-acetoxybutyl)] amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (3-cyanopropyl)] amide;

20 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (3-methoxypropyl)] amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-acetyl-amino-ethyl)] amide;

25 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [2- (2-pyridyl) -ethyl] } amide;

30 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- [2- (N-oxomorpholino) ethyl] amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [3- (tert-butylsulfonyl) -propyl] } amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [3- (ethylsulfonyl) -propyl] } -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [2- (ethylsulfonyl) -ethyl] } -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [2- (N-butylsulfonyl) -ethyl] } -amide;

10 [(S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [2- (N,N-dimethylsulfonylamino) -ethyl] } -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [3- (1H-tetrazol-5-yl) -propyl] } -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [3- (1H-imidazol-5-yl) -propyl] } -amide;

20 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [3- (3-methyl-1,2,4-oxadiazol-5-yl) -propyl] } -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (3-aminopropyl)] -amide;

25 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- [2-dimethylamino-ethyl]] -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- (2-morpholinoethyl) amide;

30 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- (3-morpholinopropyl) amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- [2- (1,1-dioxothiomorpholino) ethyl] amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- (2-ethoxycarbonyl ethyl) amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carboxy-ethyl)] -amide;

10 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (3-methoxycarbonyl-ethyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (3-carboxypropyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carbamoyl ethyl)] -amide;

20 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (4-carbamoyl butyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- {3- [N- (2-methoxyethyl) carbamoyl] propyl} amide;

25 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- (4-morpholino-4-oxo-butyl) amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carbamoyl-2,2-dimethyl-ethyl)] -amide;

30 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- (1,1-dimethyl-2-morpholino-ethyl) amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- [1 (R, S) -methyl-2-morpholino-ethyl] amide;

5 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (1-carbamoyl-1-methyl-ethyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (1-carbamoyl-methyl)] -amide;

10 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carbamoyl-ethyl)] -amide;

15 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- [2- (N-methyl-carbamoyl) ethyl] amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- (3-morpholino-3-oxo-propyl) amide;

20 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [2- (N, N-dimethyl-carbamoyl) -1 (R, S) -methyl-ethyl]} -amide;

(S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carbamoyl-1 (R) -isopropyl-ethyl)] -amide;

25 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [2- (N-methylcarbamoyl) -1 (R) -isopropyl-ethyl]} -amide;

30 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [2- (N,N-dimethylcarbamoyl) -1 (R) -isopropyl-ethyl]} -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (1 (S) -carbamoyl-2-hydroxy-ethyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (1 (S) , 2-dicarbamoyl-ethyl)] -amide;

5 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (1 (S) , 3-dicarbamoyl-propyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (1 (S) -carbamoyl-propyl)] -amide;

10 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (1 (S) -carbamoyl-2 (S) -methyl-butyl)] -amide;

15 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- [2 (R, S) -carbamoyl-2 (R, S) -methyl-ethyl] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carbamoyl-1 (S) -methyl-ethyl)] -amide;

20 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carbamoyl-1 (R) -methyl-ethyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- [2 (S) -carbamoyl-2 (S) -methylethyl] -amide;

25 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [2 (S) - (N-methyl-carbamoyl) -2 (S) -methyl-ethyl] } -amide;

30 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carboxy-2, 2-dimethyl-ethyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-carboxy-2, 2-diethyl-ethyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- [(1-carboxy-cyclopentyl) -methyl] amide;

5 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [2- (1 H-tetrazol-5-yl) -ethyl] } -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- [1 (S) - (5-oxopyrrolidin-2-yl) methyl] -amide;

10 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- [1 (R) - (5-oxopyrrolidin-2-yl) methyl] -amide;

5 (S) -amine-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- [N- (morpholin-4-yl) carbamoyl-methyl] amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (1 (S) -carbamoyl-ethyl)] -amide;

20 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- {1 (S) - [(N-methyl) -carbamoyl] -ethyl} -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- {1 (S) - [(N, N-dimethyl) -carbamoyl] -ethyl} -amide;

25 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- {1 (S) - N- [(morpholin-4-yl) -carbamoyl] -ethyl} amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- [1 (S) - carbamoylbutyl] amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid N- [1 (S) - carbamoyl-2-methyl-propyl] -amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[1 (S)-(N-methylcarbamoyl)-2-methyl-propyl]amide;

5 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[1 (S)-(N,N-dimethylcarbamoyl)-2-methyl-propyl]amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-{1 (S)-[N-(morpholin-4-yl)carbamoyl]-2-methyl-propyl}amide;

10 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[2-(N-methylsulfonylamino)ethyl]amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-{2-[N-(morpholin-4-yl)-sulfonyl]ethyl}amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[(N-acetyl-piperidin-4-yl)methyl]amide;

20 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(4-methoxy-butyl)-phenyl]-octanoic acid N-(2-carbamoyl-2,2-dimethylethyl)amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[2-(N,N-dimethylcarbamoyl)ethyl]amide;

25 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(4-methoxybutylphenyl)-octanoic acid N-(2-morpholinoethyl)amide;

and a pharmaceutically salt thereof.

30 7. A method according to claim 1, which is selected from the group consisting of:

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (3 (R) -2-oxo-pyrrolidin-3-yl-methyl)] -amide;

5 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (3 (S) -2-oxo-piperidin-3-yl-methyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (3 (R) -2-oxo-piperidin-3-yl-methyl)] -amide;

10 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyl-oxy) -phenyl] -octanoic acid [N- (3-carbamoyl-3,3-dimethyl-propyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (4-methoxy-butyl) phenyl] -octanoic acid [N- (5 (S) -2-pyrrolidinon-5-yl-methyl)] -amide;

15 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (4-methoxy-butyl) -phenyl] -octanoic acid [N- (5 (R) -2-pyrrolidinon-5-yl-methyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (6 (S) -2-oxo-piperidin-6-yl-methyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (6 (R) -2-oxo-piperidin-6-yl-methyl)] -amide;

25 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-thiazol-2-yl-ethyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (4 (S) -2-oxazolidinon-4-yl-methyl)] -amide;

30 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (4 (R) -2-oxazolidinon-4-yl-methyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (3 (S) -2.5-dioxo-pyrrolidin-3-yl-methyl)] -amide;

5 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (3 (R) -2.5-dioxo-pyrrolidin-3-yl-methyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2,6-dioxo-piperidin-4-yl-methyl)] -amide;

10 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (4 (S) -2-oxothiazolidin-4-yl-methyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (4 (R) -2-oxothiazolidin-4-yl-methyl)] -amide;

15 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (tetrahydro-2-pyrimidon-5-yl-methyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxypropyloxy) -phenyl] -octanoic acid [N- (N-acetyl-2-amino-2-methyl-propyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (N-formyl-2-amino-2-methyl-propyl)] -amide;

25 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (4-acetyl-piperazinyl-ethyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2,4-imidazolinedion-5-yl-methyl)] -amide;

30 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (4-methoxy-butyl) phenyl] -octanoic acid [N- (2-hydroxy-pyridin-6-yl-methyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2,2-dimethyl-2-sulfamoyl-ethyl)] -amide;

5 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2,2-dimethyl-2- (N,N-dimethyl) -sulfamoyl-ethyl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-oxo-piperidin-3 (R) -yl)] -amide;

10 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-oxo-piperidin-3 (S) -yl)] -amide;

15 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2-oxo-piperidin-4-yl)] -amide;

5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (N-acetyl-piperidin-4-yl)] -amide; or

20 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (4-methoxy-but-1-en-yl) -phenyl] -octanoic acid [N- (2-carbamoyl-2,2-dimethyl-ethyl)] -amide; and pharmaceutically acceptable salts thereof.

8. A method according to claim 1 wherein the compound is
25 5 (S) -Amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxypropyloxy) -phenyl] -octanoic acid morpholinopropyl) amide or a pharmaceutically acceptable salt thereof.

9. A method according to claim 1 wherein the compound is
30 5 (S) -Amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-3- (3-methoxypropyloxy) -phenyl] -octanoic acid morpholinoethyl) amide or a pharmaceutically acceptable salt thereof.

10. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-
methoxypropyloxy)-phenyl]-octanoic acid {N-[2-(N-methyl-
carbamoyl)-1(R,S)-methyl-ethyl]}-amide or a pharmaceutically
5 acceptable salt thereof.

11. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-
methoxypropyloxy)-phenyl]-octanoic acid N-(3-
10 carbamoylpropyl)amide or a pharmaceutically acceptable salt
thereof.

12. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-
15 methoxypropyloxy)-phenyl]-octanoic acid {N-[2(R)-(N-methyl-
carbamoyl)-2(R)-methyl-ethyl]}-amide or a pharmaceutically
acceptable salt thereof.

13. A method according to claim 1 wherein the compound is
20 5 (S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-
methoxypropyloxy)-phenyl]-octanoic acid N-(2-
thiomorpholinoethyl)amide or a pharmaceutically acceptable salt
thereof.

25 14. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-
methoxypropyloxy)-phenyl]-octanoic acid N-[2-(N,N-dimethyl-
carbamoyl)ethyl]amide or a pharmaceutically acceptable salt
thereof.

30

15. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-
methoxypropyloxy)-phenyl]-octanoic acid N-(2-carbamoyl-1(R,S)-

methyl-ethyl)amide or a pharmaceutically acceptable salt thereof.

16. A method according to claim 1 wherein the compound is
5 5(S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid N-[2(R)-carbamoyl-2(R)-methyl-ethyl]-amide or a pharmaceutically acceptable salt thereof.

10 17. A method according to claim 1 wherein the compound is 5(S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid N-(2-carbamoyl-2,2-dimethyl-ethyl)amide or a pharmaceutically acceptable salt thereof.

15 18. A method according to claim 1 wherein the compound is 5(S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid N-[2-(N-acetyl)-piperidin-4-yl)ethyl]amide or a pharmaceutically acceptable salt
20 thereof.

19. A method according to claim 1 wherein the compound is 5(S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid {N-[(N,N-dimethyl)-
25 carbamoyl-methyl]}-amide or a pharmaceutically acceptable salt thereof.

20. A method according to claim 1 wherein the compound is 5(S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid N-[2(R,S)-(N-methylcarbamoyl)-2(R,S)-methyl-ethyl]-amide or
30 a pharmaceutically acceptable salt thereof.

21. A method according to claim 1 wherein the compound is
 5 (S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid N-(2-carbamoyl-2,2-dimethyl-ethyl)-amide or a pharmaceutically acceptable salt thereof.

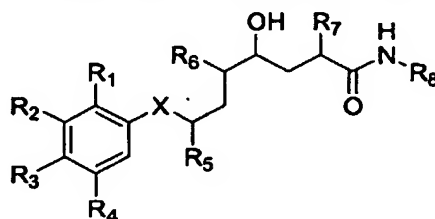
22. A method according to claim 1 wherein the compound is
 10 (S)-Amino-2(S),7(S)-diisopropyl-4(S)-hydroxy-8-[4-tert-butyl-3-(3-methoxypropoxy)-phenyl]-octanoic acid [N-2-(morpholin-4-yl)-ethyl]-amide or a pharmaceutically acceptable salt thereof.

23. A method according to claim 1, wherein the subject is a human.

15 24. A method according to claim 1, wherein the disease is dementia.

25 25. A method according to claim 1, wherein the disease is Alzheimer's disease.

26. A method for making a compound of the formula



wherein

25 R₁ is hydrogen, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy or free or esterified or amidated carboxy-lower alkoxy;

R₂ is hydrogen, lower alkyl, cycloalkyl, lower alkoxy-lower alkyl, lower alkoxy-lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, hydroxy, optionally lower alkanoylated,

halogenated or sulfonylated hydroxy-lower alkoxy; amino-lower alkyl that is unsubstituted or substituted by lower alkyl, by lower alkanoyl and/or by lower alkoxycarbonyl; optionally hydrogenated heteroaryl-lower alkyl; amino-lower alkoxy that is substituted by lower alkyl, by lower alkanoyl and/or by lower alkoxycarbonyl; oxo-lower alkoxy, lower alkoxy, cycloalkoxy, lower alkenyloxy, cycloalkoxy-lower alkoxy, lower alkoxy-lower alkoxy, lower alkoxy-lower alkenyl, lower alkenyloxy-lower alkoxy, lower alkoxy-lower alkenyloxy, lower alkenyloxy-lower alkyl, lower alkanoyl-lower alkoxy, optionally S-oxidised lower alkylthio-lower alkoxy, lower alkylthio-(hydroxy)-lower alkoxy, aryl-lower alkoxy, optionally hydrogenated heteroaryl-lower alkoxy, cyano-lower alkoxy, free or esterified or amidated carboxy-lower alkoxy or free or esterified or amidated carboxy-lower alkyl;

R₃ is halogenated lower alkyl, lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, hydroxy-lower alkyl, optionally S-oxidised lower alkylthio-lower alkyl, optionally hydrogenated heteroarylthio-lower alkyl, optionally hydrogenated heteroaryl-lower alkyl; amino-lower alkyl that is unsubstituted or N-mono- or N,N-di-lower alkylated. N-lower alkanoylated or N-lower alkane-sulfonylated or N,N-disubstituted by lower alkylene, by unsubstituted or N'-lower alkylated or N'-lower alkanoylated aza-lower alkylene, by oxa-lower alkylene or by optionally S-oxidised thia-lower alkylene; cyano-lower alkyl, free or esterified or amidated carboxy-lower alkyl, cycloalkyl, aryl, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, cycloalkoxy-lower alkoxy, hydroxy-lower alkoxy, aryl-lower alkoxy, optionally halogenated lower alkoxy, optionally S-oxidised lower alkylthio-lower alkoxy, optionally hydrogenated heteroaryl-lower alkoxy, optionally

hydrogenated heteroarylthio-lower alkoxy; amino-lower alkoxy that is unsubstituted or N-mono- or N,N-di-lower alkylated. N-lower alkanoylated or N-lower alkanesulfonylated or substituted by lower alkylene, by
5 unsubstituted or N'-lower alkylated or N'-lower alkanoylated aza-lower alkylene, by oxa-lower alkylene or by optionally S-oxidised thia-lower alkylene; cyano-lower alkoxy or free or esterified or amidated carboxy-lower alkoxy;

10 R_4 is hydrogen, lower alkyl, hydroxy, lower alkoxy or cycloalkoxy;

X is methylene;

R_5 is lower alkyl or cycloalkyl;

R_6 is unsubstituted or N-mono- or N,N-di-lower alkylated or N-
15 lower alkanoylated amino;

R_7 is lower alkyl, lower alkenyl, cycloalkyl or aryl-lower alkyl; and

R_8 is lower alkyl, cycloalkyl, free or aliphatically esterified or etherified hydroxy-lower alkyl; amino-lower alkyl that
20 is unsubstituted or N-lower alkanoylated or N-mono- or N,N-di-lower alkylated or N,N-disubstituted by lower alkylene, by hydroxy- lower alkoxy- or lower alkanoyloxy-lower alkylene, by unsubstituted or N'-lower alkanoylated or N'-lower alkylated aza-lower alkylene, by oxa-lower alkylene
25 or by optionally S-oxidised thia-lower alkylene; free or esterified or amidated carboxy-lower alkyl, free or esterified or amidated dicarboxy-lower alkyl, free or esterified or amidated carboxy-(hydroxy)-lower alkyl, free or esterified or amidated carboxycycloalkyl-lower alkyl,
30 cyano-lower alkyl, lower alkanesulfonyl-lower alkyl, unsubstituted or N-mono- or N,N-di-lower alkylated thiocarbamoyl-lower alkyl, unsubstituted or N-mono- or N,N-di-lower alkylated sulfamoyl-lower alkyl, or a heteroaryl

radical bonded via a carbon atom and optionally hydrogenated and/or oxo-substituted, or lower alkyl substituted by a heteroaryl radical bonded via a carbon atom and optionally hydrogenated and/or oxo-substituted, or
5 a pharmaceutically acceptable salt thereof.